Remarks

The Office Action mailed October 28, 2002 has been received and reviewed. Claims 1, 3, and 9-12, and 21-40 having been amended, the pending claims are claims 1-4, 9-12, and 21-44. Support for the amendments to the claims is found throughout the specification and in the claims as originally filed. For example, support for the recitation "nuclear and mitochondrial" in amended claims 1, 3, and 9-12, and 21-40 is found on page 13, line 22-24, and page 14, lines 6-7, of the specification, and support for the recitation "60%" in amended claims 1, 3, 11, 12, and 21-40 is found at page 12, lines 14-16, of the specification. Reconsideration and withdrawal of the rejections is respectfully requested.

Request for Rejoinder

Applicants maintain their request for the rejoinder and examination of previously withdrawn claims 21-40, pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86).

Examiner Interview

A telephonic Examiner Interview was held on January 21, 2003 between Applicants' Representative and Patent Examiner Malgorzata Walicka and Primary Patent Examiner Rebecca Prouty of the U.S. Patent and Trademark Office. At this interview the rejections under 35 U.S.C. §112, first paragraph, and the objection to the specification were discussed. Patent Examiners Walicka and Prouty are thanked for the courtesy of this interview.

Withdrawn Rejections

Applicants note with appreciation the withdrawal of the following rejections: the rejection of claims 1-4 and 9-12 under 35 USC § 101; the rejection of claim 9 and 10 under 35

USC §112, first paragraph (lack of written description); the rejection of claims 1 and 2 under 35 USC §102 as anticipated by Nilsen et al.; and the rejection of claims 9 and 10 under 35 USC § 103 as unpatentable over any one of Lu et al., Valerie et al. or Pierson et al., each in view of Nilsen et al. or Otterlai et al.

Objection to the Specification

The Examiner maintained the objection to the disclosure for containing an embedded hyperlink. The specification has been amended to recite "available on the worldwide web at ncbi.nlm.nih.gov.gorf/b12.html." Withdrawal of this objection to the specification is respectfully requested.

The 35 U.S.C. §112, First Paragraph, Written Description Rejection

The Examiner rejected claims 1-4, 11, 12, 43, and 44 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserted that although polypeptides with SEQ ID NOs: 41, 42 and 43 are described in the specification, as the Applicants have failed "to describe any amino acid sequence identifying a polypeptide having a glycosylase activity and 15% identity to any one of SEQ ID Nos: 41, 42 and 43 . . . one skilled in the art is not convinced that at the time the application was filed Applicants were in possession of the claimed invention" (Page 3 of the Office Action mailed October 28, 2002).

This rejection is respectfully traversed. The Examiner's position appears to be that the written description requirement of 35 U.S.C. §112, first paragraph, is met only by the actual reduction to practice of each and every species encompassed by the scope of the claim. This is an incorrect application of the written description requirement. The Office Action (pg. 9) also states that the specification fails to teach a structure/function relationship for enzymes having

amino acid sequences of SEQ ID NO: 41,42 and 43. This, too, is a mistatement of the written description requirement. To meet the written description requirement of 35 U.S.C. §112, first paragraph, the application "must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, i.e., what is now claimed." M.P.E.P. § 2163. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention, not just "a structure/function relationship" as asserted by the Examiner. "Disclosure of any combination of such identifying characteristics that distinguish the claimed inventions from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406.

Claims 1-4, 11, 12, 43, and 44 are drawn to isolated polypeptides that 1) have an amino acid sequence having at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and 2) have pyrimidine glycosylase activity (claims 1-4) or pyrimidine glycosylase /AP lyase activity (claims 11 and 12). Thus, the polypeptides of claims 1-4, 11, 12, 43, and 44 are claimed by both a physical characteristic (having an amino acid sequence at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43) and a functional characteristic (having pyrimidine glycosylase or pyrimidine glycosylase /AP lyase activity).

Applicants respectfully submit that adequate written description is provided for claims 1-4, 11, 12, 43, and 44. The specification provides detailed information for making polypeptides with the claimed physical characteristics of the polypeptides of claims 1-4, 11, 12, 43, and 44. The specification provides the amino acid sequences of SEQ ID NO:41, SEQ ID NO:42 and SEQ ID NO:43 (see, for example, Figure 24), and also provides detailed instructions for making polypeptides with an amino acid sequence having at least about 60% identity with those amino

acid sequences. See p. 11, line 15 - p. 12, line 16 of the specification. Likewise, the specification provides complete information for making polypeptides with the claimed functional characteristics, i.e., having pyrimidine glycosylase or pyrimidine glycosylase /AP lyase activity. See, for example, p.8, lines 14-24; p. 9, line 19 - p. 10, line 26; p. 43, line 24- p. 44, line 22; and p. 52, line 17 - p. 53, line 15 of the specification

Applicants respectfully submit the present specification conveys with reasonable clarity to those skilled in the art that, as of the filing date, Applicants were in possession of the invention. Applicants respectfully maintain that they have satisfied the written description requirement for claims 1-4, 11, 12, 43, and 44. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, are respectfully requested.

The 35 U.S.C. §112, First Paragraph, Enablement Rejection of claims 1-4, 11, 12, 43 and 44

The Examiner rejected claims 1-4, 11, 12, 43, and 44 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

Claims 1-4, 11-12, and 43-44 are drawn to isolated polypeptides that have an amino acid sequence having at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and have pyrimidine glycosylase activity (claims 1-4) or pyrimidine glycosylase /AP lyase activity (claims 11, 12, 43, and 44). It is respectfully submitted that the specification provides detailed information for making polypeptides with the claimed physical characteristics i.e., polypeptides having at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43. See p. 11, line 15 - p. 12, line 16 of the specification. Likewise, the specification provides detailed information for making polypeptides with the claimed functional characteristics, i.e., pyrimidine glycosylase or pyrimidine glycosylase /AP lyase activity. See, for example, p.8, lines 14-24; p. 9, line 19 - p. 10, line 26; p.

43, line 24– p. 44, line 22; and p. 52, line 17 - p. 53, line 15 of the specification. Additionally, with SEQ ID NO:41, 43 and 43, the specification provides several working examples. And, as the Examiner has acknowledged, the level of skill in the relevant art is high, as the techniques of "gene cloning, sequencing, manipulations, expressing in host cells, isolating proteins from host cells, measuring enzymatic activity and protein sequencing are well known" (see p. 6 of Office Action mailed May 22, 2002).

Thus, in order to make the claimed polypeptide, one skilled in the art need only, for example, (a) isolate or synthesize a candidate polypeptide; (b) sequence the candidate polypeptide to determine if the candidate polypeptide has at least about 60% identity with the amino acid sequence of SEQ ID NO:41, 42 or 43; and (c) conduct a straightforward enzymatic assay to determine whether the candidate polypeptide has pyrimidine glycosylase or pyrimidine glycosylase /AP lyase activity. None of these steps involves undue experimentation, and all are within the ordinary skill of an art worker in the field.

It is respectfully submitted that the present specification provides sufficient guidance to one of skill in the art to identifying the claimed polypeptides; polypeptides having at least about 60% identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43 (see p. 11, line 15 - p. 12, line 16 of the specification) and having pyrimidine glycosylase or pyrimidine glycosylase /AP lyase activity (see, for example, p.8, lines 14-24; p. 9, line 19 - p. 10, line 26; p. 43, line 24– p. 44, line 22; and p. 52, line 17 - p. 53, lines 15-16 of the specification). This guidance is sufficient to allow one of skill in the art to identify the claimed polypeptides with only routine experimentation. It does not require undue experimentation to practice the claimed invention commensurate with the scope of the claims. Withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

The New 35 U.S.C. §112, First Paragraph, Enablement Rejection

The Examiner rejected claims 1-4, 9-12, and 41-44 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner asserted that while enabling for mitochondrial localization sequences and nuclear localization sequences, the specification does not reasonably provide enablement for the many other types of targeting sequences in living cells. This rejection is respectfully traversed. The polypeptides of claims 1-4, 9-12, and 41-44 comprise a nuclear or mitochondrial targeting sequence. It is respectfully submitted that the present specification provides sufficient guidance to one of skill in the art to make and use the claimed polypeptides; polypeptides comprising a nuclear or mitochondrial targeting sequence. Withdrawal of this rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

It is noted that on page 11 of the Office Action mailed October 28, 2002, the Examiner suggested "limiting the scope of some claims to human mitochondrial and nuclear localization sequences." Applicants respectfully disagree with this suggestion. Mitochondrial and nuclear localization sequences are highly conserved between humans and other species. Thus, Applicants submit that there is no need to limit the claimed invention to human sequences.

Summary

It is respectfully submitted that the pending claims 1-4, 9-12, and 21-44 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on this 28th day of January, 2003, at 2:00pm (Central Time).

By: Sara E. Olson
Name: SARA E. OLSON

APPENDIX A - SPECIFICATION/CLAIM AMENDMENTS INCLUDING NOTATIONS TO INDICATE CHANGES MADE
Serial No.: 09/864,866
Docket No.: 265.00170101

Amendments to the following are indicated by underlining what has been added and bracketing what has been deleted. Additionally, all amendments have been shaded.

In the Specification

The paragraph beginning at page 11, line 15, has been amended as follows:

The present invention further includes polypeptides having pyrimidine glycosylase activity, preferably pyrimidine glycosylase/AP lyase activity, and amino acid identity with the amino acid sequence of SEQ ID NO:41, SEQ ID NO:42, or SEQ ID NO:43, preferably SEQ ID NO:41 or SEQ ID NO:42. Amino acid identity is defined in the context of a comparison between a polypeptide and SEQ ID NO:41 or SEQ ID NO:42, and is determined by aligning the residues of the two amino acid sequences (i.e., a candidate amino acid sequence and the amino acid sequence of SEQ ID NO:41, SEQ ID NO:42, or SEQ ID NO:43) to optimize the number of identical amino acids along the lengths of their sequences; gaps in either or both sequences are permitted in making the alignment in order to optimize the number of identical amino acids, although the amino acids in each sequence must nonetheless remain in their proper order. A candidate amino acid sequence is the amino acid sequence being compared to an amino acid sequence present in SEQ ID NO:41, SEQ ID NO:42, or SEQ ID NO:43. A candidate amino acid sequence can be isolated from a microbe or a microbe harboring a virus, or can be produced using recombinant techniques, or chemically or enzymatically synthesized. Preferably, two amino acid sequences (i.e., the candidate amino acid sequence and the amino acid sequence present in SEQ ID NO:41, SEQ ID NO:42, or SEQ ID NO:43) are compared using the Blastp program of the BLAST 2 search algorithm, as described by Tatusova, et al. (*FEMS Microbiol Lett* 1999, 174:247-250), [and available at www.ncbi.nlm.nih.gov/gorf/bl2.html] and available on the worldwide web at ncbi.nlm.nih.gov.gorf/b12.html. Preferably, the default values for all BLAST 2 search parameters are used, including matrix = BLOSUM62; open gap penalty = 11, extension gap penalty = 1, gap x_dropoff = 50, expect = 10, wordsize = 3, and filter on. In the comparison of two amino acid sequences using the BLAST search algorithm, amino acid identity

is referred to as "identities." Preferably, a polypeptide having pyrimidine glycolase activity has an amino acid sequence having, in increasing order of preference, at least about 15 % amino acid identity, at least about 30 % amino acid identity, at least about 40 % amino acid identity, at least about 50 % amino acid identity, and most preferably, at least about 60 % amino acid identity to SEQ ID NO:41, SEQ ID NO:42, or SEQ ID NO:43.

In the Claims

For convenience, all pending claims are shown below.

1. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence having pyrimidine glycosylase activity, the amino acid sequence having at least about 60% [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

a nuclear or mitochondrial targeting sequence.

2. A composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable carrier.

3. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence having pyrimidine glycosylase activity, the amino acid sequence having at least about 60% [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

an exogenous nuclear or mitochondrial targeting sequence.

4. A composition comprising the polypeptide of claim 3 and a pharmaceutically acceptable carrier.

9. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

a nuclear or mitochondrial targeting sequence.

10. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

an exogenous nuclear or mitochondrial targeting sequence.

11. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence having pyrimidine glycosylase/AP lyase activity, the amino acid sequence having at least about 60% [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

a nuclear or mitochondrial targeting sequence.

12. [TWICE AMENDED] An isolated polypeptide comprising:

an amino acid sequence having pyrimidine glycosylase /AP lyase activity, the amino acid sequence having at least about 60% [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43; and

an exogenous nuclear or mitochondrial targeting sequence.

21. [TWICE AMENDED] A method for increasing the repair rate of damaged bases in a cell, the method comprising introducing to a cell exposed to or at risk of exposure to an agent that damages DNA a composition comprising an amount of an isolated polypeptide effective to increase the repair rate of damaged DNA in the cell compared to a cell that does not comprise the polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID

NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

22. [TWICE AMENDED] A method for increasing the repair rate of damaged bases in a cell, the method comprising introducing to a cell exposed to or at risk of exposure to an agent that damages DNA a composition comprising an amount of an isolated polypeptide effective to increase the repair rate of damaged DNA in the cell compared to a cell that does not comprise the polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

23. [TWICE AMENDED] A method for increasing the repair rate of damaged bases in a cell, the method comprising introducing to a cell exposed to or at risk of exposure to an agent that damages DNA a composition comprising an amount of an isolated polypeptide effective to increase the repair rate of damaged DNA in the cell compared to a cell that does not comprise the polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

24. [TWICE AMENDED] A method for increasing the repair rate of damaged bases in a cell, the method comprising introducing to a cell exposed to or at risk of exposure to an agent that damages DNA a composition comprising an amount of an isolated polypeptide effective to increase the repair rate of damaged DNA in the cell compared to a cell that does not comprise the polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine

glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

25. [TWICE AMENDED] A method for treating mutagenesis in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an nuclear or mitochondrial targeting sequence.

26. [TWICE AMENDED] A method for treating mutagenesis in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

27. [TWICE AMENDED] A method for treating mutagenesis in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID

NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

28. [TWICE AMENDED] A method for treating mutagenesis in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

29. [TWICE AMENDED] A method for treating immunosuppression in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

30. [TWICE AMENDED] A method for treating immunosuppression in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ

ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

31. [TWICE AMENDED] A method for treating immunosuppression in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

32. [TWICE AMENDED] A method for treating immunosuppression in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

33. [TWICE AMENDED] A method for treating tumor formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

34. [TWICE AMENDED] A method for treating tumor formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

35. [TWICE AMENDED] A method for treating tumor formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

36. [TWICE AMENDED] A method for treating tumor formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

37. [TWICE AMENDED] A method for treating apoptotic cell formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

38. [TWICE AMENDED] A method for treating apoptotic cell formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

39. [TWICE AMENDED] A method for treating apoptotic cell formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises a nuclear or mitochondrial targeting sequence.

40. [TWICE AMENDED] A method for treating apoptotic cell formation in a subject, the method comprising introducing to a subject exposed to or at risk of exposure to an agent that damages DNA a composition comprising an effective amount of an isolated polypeptide, wherein the polypeptide comprises an amino acid sequence having pyrimidine glycosylase/AP lyase activity, wherein the amino acid sequence has at least about 60 % [15 %] identity with an amino acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, and SEQ ID NO:43, and wherein the polypeptide further comprises an exogenous nuclear or mitochondrial targeting sequence.

41. A composition comprising the polypeptide of claim 9 and a pharmaceutically acceptable carrier.

42. A composition comprising the polypeptide of claim 10 and a pharmaceutically acceptable carrier.

43. A composition comprising the polypeptide of claim 11 and a pharmaceutically acceptable carrier.

44. A composition comprising the polypeptide of claim 12 and a pharmaceutically acceptable carrier.